FILE 'HOME' ENTERED AT 12:54:01 ON 08 OCT 2003

=> index bioscience
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 12:54:17 ON 08 OCT 2003

67 FILES IN THE FILE LIST IN STNINDEX

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=> s (alveolit? or interstit?(2a)lung?(2a)diseas? or ILD) and resveratrol?
          2   FILE CAPLUS
  23 FILES SEARCHED...
  32 FILES SEARCHED...
          2   FILE FROSTI
  51 FILES SEARCHED...
          1   FILE WPIDS
          1   FILE WPINDEX

   4 FILES HAVE ONE OR MORE ANSWERS,   67 FILES SEARCHED IN STNINDEX

L2   QUE (ALVEOLIT? OR INTERSTIT?(2A) LUNG?(2A) DISEAS? OR ILD) AND RESVERATROL
        ?

=> file caplus, frosti, wpids, wpindex
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FILE 'CAPLUS' ENTERED AT 12:58:52 ON 08 OCT 2003
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=> s l2
L3            5 L2

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4             4 DUP REM L3 (1 DUPLICATE REMOVED)

=> d l4 abs ibib kwic 1-4

L4   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2003 ACS on STN
AB   The invention is concerned with the use of lycopene, optionally in
     combination with vitamin E and/or C or other biol. active ingredients as
     disclosed in the specification, in the manuf. of a compn. for the primary
     and secondary prevention of angiogenesis-assocd. pathologies and
     coadjuvant treatment thereof, as well as with particular novel
     formulations comprising lycopene.  A tablet for the coadjuvant treatment
     of prostate carcinoma is formulated to contain 5 mg of lycopene, 200 mg of
     vitamin E, 250 mg of vitamin C, 37.5 mg of resveratrol, and 50
     mg of quercetin.  The daily dosage is two such tablets.
ACCESSION NUMBER:         2003:656555  CAPLUS
DOCUMENT NUMBER:          139:202483
TITLE:                    Compositions comprising lycopene for the treatment and
                          prevention of angiogenesis associated pathologies
INVENTOR(S):              Barella, Luca; Goralczyk, Regina; Jung, Klaus; Lein,
                          Michael; Siler, Ulrich; Stoecklin, Elisabeth; Wertz,
                          Karin
PATENT ASSIGNEE(S):       Roche Vitamins A.-G., Switz.; Humboldt Universitaet
SOURCE:                   PCT Int. Appl., 27 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2003068202      A1   20030821       WO 2003-EP1149   20030206
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
             UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
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CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2002-3544 A 20020215

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The invention is concerned with the use of lycopene, optionally in combination with vitamin E and/or C or other biol. active ingredients as disclosed in the specification, in the manuf. of a compn. for the primary and secondary prevention of angiogenesis-assocd. pathologies and coadjuvant treatment thereof, as well as with particular novel formulations comprising lycopene. A tablet for the coadjuvant treatment of prostate carcinoma is formulated to contain 5 mg of lycopene, 200 mg of vitamin E, 250 mg of vitamin C, 37.5 mg of **resveratrol**, and 50 mg of quercetin. The daily dosage is two such tablets.

IT **Lung, disease**
(fibrosis, **interstitial**; compns. comprising lycopene for treatment and prevention of angiogenesis assocd. pathologies)

IT 50-14-6, Vitamin D2 50-81-7, Vitamin c, biological studies 57-06-7, Allyl isothiocyanate 57-87-4, Ergosterol 67-97-0, Vitamin D3 68-26-8, all-Trans-Retinol 79-81-2, Retinyl palmitate 117-39-5, Quercetin 127-40-2, Lutein 127-47-9, Retinyl acetate 144-68-3, Zeaxanthin 446-72-0, Genistein 446-72-0D, Genistein, aglycons 458-37-7, Curcumin 472-61-7, Astaxanthin 472-70-8, .beta.-Cryptoxanthin 491-70-3, Luteolin 499-30-9, Gluconasturtiin 499-37-6 501-36-0, **Resveratrol** 502-65-8, Lycopene 505-44-2, 3-Methylsulfinylpropyl isothiocyanate 520-36-5, Apigenin 528-48-3, Fisetin 529-44-2, Myricetin 554-88-1, (Glucoiberin) 646-23-1, 5-Methylsulfinyl-pentyl isothiocyanate 700-06-1, 1H-Indole-3-methanol 961-29-5, Isoliquiritigenin 989-51-5, (-)-Epigallocatechin gallate 1257-08-5 1406-18-4, Vitamin E 2257-09-2, Phenylethyl isothiocyanate 3386-97-8, 3-Butenyl isothiocyanate 3650-09-7, Carnosic acid 3952-98-5, (Sinigrin 4356-52-9, (Glucobrassicin 4430-35-7 4478-93-7, (Sulforaphane 5041-81-6, Isoliquiritin 5187-84-8, (Neoglucobrassicin 5957-80-2, Carnosol 7235-40-7, .beta.-Carotene 12772-57-5, Radicicol 19041-09-9, Gluconapin 19356-17-3, 25-Hydroxyvitamin D3 19683-98-8, Ovalicin 21414-41-5, Glucoraphanin 21973-60-4, 8-Methylsulfinyloctyl glucosinolate 22888-70-6, Silybin 23110-15-8, Fumagillin 29782-68-1, Silydianin 32222-06-3, 1.alpha.,25-Dihydroxy-vitamin D3 33049-17-1, 6-Methylsulfinylhexyl glucosinolate 33889-69-9, Silychristin) 56142-94-0 65666-07-1, Silymarin 67884-10-0 67920-64-3, 9-Methylsulfinylnonyl glucosinolate 72581-71-6, Isosilybin 75272-81-0 75272-82-1 75272-83-2 77012-75-0, Indol-3-ylmethylisothiocyanate 83327-20-2, 4-Hydroxy glucobrassicin 83327-21-3, 4-Methoxy glucobrassicin 90996-54-6, Rhizoxin 112572-51-7, 7-Methylsulfinylheptyl glucosinolate 126463-64-7, Dihydroeponemycin 126509-46-4, Eponemycin 126769-93-5 129244-98-0 133343-34-7, Lactacystin 134381-21-8, Epoxomicin 135819-69-1 139508-73-9, Depudecin 148717-90-2, Squalamine 206443-55-2 211569-34-5, Motuporamine C 443340-10-1, 2-Methylsulfinylethyl glucosinolate 582304-76-5 582304-79-8 582304-81-2 582304-82-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising lycopene for treatment and prevention of angiogenesis assocd. pathologies)

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1

AB A method is provided for treating inflammatory respiratory disorders such as asthma and chronic obstructive pulmonary disease (COPD). The method involves administration, preferably oral or pulmonary administration, of an active agent selected from the group consisting of **resveratrol**, pharmacol. acceptable salts, esters, amides, prodrugs and analogs thereof, and combinations of any of the foregoing. Pharmaceutical formulations for use in conjunction with the aforementioned method are provided as well.

ACCESSION NUMBER: 2002:314756 CAPLUS
DOCUMENT NUMBER: 136:319401
TITLE: Administration of **resveratrol** to treat inflammatory respiratory disorders
INVENTOR(S): Donnelly, Louise Elizabeth; Barnes, Peter John
PATENT ASSIGNEE(S): Imperial College Innovations Limited, UK
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032410	A2	20020425	WO 2001-GB4672	20011019
WO 2002032410	A3	20020801		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001095760	A5	20020429	AU 2001-95760	20011019
EP 1326595	A2	20030716	EP 2001-976492	20011019
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-694108 A 20001019
WO 2001-GB4672 W 20011019

TI Administration of **resveratrol** to treat inflammatory respiratory disorders
AB A method is provided for treating inflammatory respiratory disorders such as asthma and chronic obstructive pulmonary disease (COPD). The method involves administration, preferably oral or pulmonary administration, of an active agent selected from the group consisting of **resveratrol**, pharmacol. acceptable salts, esters, amides, prodrugs and analogs thereof, and combinations of any of the foregoing. Pharmaceutical formulations for use in conjunction with the aforementioned method are provided as well.

ST inflammatory respiratory disorder **resveratrol**
IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NF-.kappa.B (nuclear factor of .kappa. light chain gene enhancer in B-cells); **resveratrol** treatment of inflammatory respiratory disorders)
IT Lung, disease
(**alveolitis**; **resveratrol** treatment of inflammatory

respiratory disorders)
IT Lung
(alveolus; **resveratrol** treatment of inflammatory respiratory disorders)
IT Macrolides
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibiotics; **resveratrol** treatment of inflammatory respiratory disorders)
IT Occupational diseases
(asthma; **resveratrol** treatment of inflammatory respiratory disorders)
IT Bronchi, disease
(chronic bronchitis; **resveratrol** treatment of inflammatory respiratory disorders)
IT Lung, disease
(chronic obstructive; **resveratrol** treatment of inflammatory respiratory disorders)
IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inflammatory; **resveratrol** treatment of inflammatory respiratory disorders)
IT Leukotriene receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **resveratrol** treatment of inflammatory respiratory disorders)
IT Antibiotics
(macrolide; **resveratrol** treatment of inflammatory respiratory disorders)
IT Anti-inflammatory agents
(nonsteroidal; **resveratrol** treatment of inflammatory respiratory disorders)
IT Asthma
(occupational; **resveratrol** treatment of inflammatory respiratory disorders)
IT Drug delivery systems
(oral; **resveratrol** treatment of inflammatory respiratory disorders)
IT Drug delivery systems
(parenterals; **resveratrol** treatment of inflammatory respiratory disorders)
IT Drug delivery systems
(pulmonary; **resveratrol** treatment of inflammatory respiratory disorders)
IT Antiasthmatics
Asthma
Bronchodilators
Concrete
Dust
Emphysema
Flours and Meals
Human
Tobacco smoke
Wood
(**resveratrol** treatment of inflammatory respiratory disorders)
IT Allergens
Asbestos
Bituminous coal

Clays, biological studies
Lime (chemical)
Polymers, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(**resveratrol** treatment of inflammatory respiratory disorders)

IT Interleukin 8
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**resveratrol** treatment of inflammatory respiratory disorders)

IT Glucocorticoids
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**resveratrol** treatment of inflammatory respiratory disorders)

IT Adrenoceptor agonists
(.beta.2-; **resveratrol** treatment of inflammatory respiratory disorders)

IT 125978-95-2, Nitric oxide synthase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inducible; **resveratrol** treatment of inflammatory respiratory disorders)

IT 9040-59-9, Cyclic nucleotide phosphodiesterase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **resveratrol** treatment of inflammatory respiratory disorders)

IT 57-50-1, Sugar, biological studies 7440-41-7, Beryllium, biological studies 7440-44-0, Carbon, biological studies 7631-86-9, Silica, biological studies 9004-34-6, Cellulose, biological studies 9005-25-8, Starch, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(**resveratrol** treatment of inflammatory respiratory disorders)

IT 83869-56-1, Granulocyte-macrophage colony-stimulating factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**resveratrol** treatment of inflammatory respiratory disorders)

IT 50-02-2, Dexamethasone 50-23-7, Hydrocortisone 58-55-9, Theophylline, biological studies 501-36-0, trans-**Resveratrol** 27208-80-6 51333-22-3, Budesonide 61434-67-1, cis-**Resveratrol** 94749-08-3, Salmeterol xinafoate 107032-81-5 148766-36-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**resveratrol** treatment of inflammatory respiratory disorders)

L4 ANSWER 3 OF 4 FROSTI COPYRIGHT 2003 LFRA on STN
AN 584005 FROSTI
AB A composition comprising **resveratrol** and its analogue is useful in the treatment of inflammatory respiratory disorders such as bronchitis, asthma, cystic fibrosis, bronchiectasis and **interstitial lung diseases**. It can be given by oral or pulmonary administration and is claimed to be more effective than oral, parenteral or pulmonary administration of corticosteroids. **Resveratrol** has known activity in as a cancer chemopreventive agent.

TITLE: Administration of **resveratrol** to treat inflammatory respiratory disorders.
INVENTOR: Donnelly L.E.; Barnes P.J.
PATENT ASSIGNEE: Imperial College Innovations Ltd
SOURCE: PCT Patent Application
PATENT INFORMATION: WO 2002032410 A2 20020425
APPLICATION INFORMATION: 20011019
PRIORITY INFORMATION: United States 20001019

NOTE: 20020425
DOCUMENT TYPE: Patent
LANGUAGE: English
SUMMARY LANGUAGE: English
TI Administration of **resveratrol** to treat inflammatory respiratory disorders.
AB A composition comprising **resveratrol** and its analogue is useful in the treatment of inflammatory respiratory disorders such as bronchitis, asthma, cystic fibrosis, bronchiectasis and **interstitial lung diseases**. It can be given by oral or pulmonary administration and is claimed to be more effective than oral, parenteral or pulmonary administration of corticosteroids. **Resveratrol** has known activity in as a cancer chemopreventive agent.
CT FUNCTIONAL FOODS; HEALTH; INFLAMMATORY RESPIRATORY DISORDERS; PATENT; PCT PATENT; RESPIRATORY DISORDERS; **RESVERATROL**

L4 ANSWER 4 OF 4 FROSTI COPYRIGHT 2003 LFRA on STN
AN 616372 FROSTI
AB A composition comprising **resveratrol** and its analogue is useful in the treatment of inflammatory respiratory disorders such as bronchitis, asthma, cystic fibrosis, bronchiectasis and **interstitial lung diseases**. It can be given by oral or pulmonary administration and is claimed to be more effective than oral, parenteral or pulmonary administration of corticosteroids. **Resveratrol** has known activity in as a cancer chemopreventive agent.
TITLE: Pharmaceutical composition comprising **resveratrol** for treating inflammatory respiratory disorders.
INVENTOR: Donnelly L.E.; Barnes P.J.
PATENT ASSIGNEE: Imperial College Innovations Ltd
SOURCE: European Patent Application
PATENT INFORMATION: EP 1326595 A2
WO 2002032410 20020425
APPLICATION INFORMATION: 20011019
PRIORITY INFORMATION: United States 20001019
DOCUMENT TYPE: Patent
LANGUAGE: English
SUMMARY LANGUAGE: English
TI Pharmaceutical composition comprising **resveratrol** for treating inflammatory respiratory disorders.
AB A composition comprising **resveratrol** and its analogue is useful in the treatment of inflammatory respiratory disorders such as bronchitis, asthma, cystic fibrosis, bronchiectasis and **interstitial lung diseases**. It can be given by oral or pulmonary administration and is claimed to be more effective than oral, parenteral or pulmonary administration of corticosteroids. **Resveratrol** has known activity in as a cancer chemopreventive agent.
CT EUROPEAN PATENT; FUNCTIONAL FOODS; HEALTH; INFLAMMATORY RESPIRATORY DISORDERS; PATENT; RESPIRATORY DISORDERS; **RESVERATROL**

=>

FILE 'HOME' ENTERED AT 14:40:25 ON 08 OCT 2003

=> index bioscience
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 14:40:48 ON 08 OCT 2003

67 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s (sarcoidio? or fibro?(3a)lung) and resveratrol?
```
          5   FILE BIOSIS
          1   FILE CABA
          1   FILE CANCERLIT
          3   FILE CAPLUS
          1   FILE DDFU
  24 FILES SEARCHED...
          1   FILE DRUGU
          1   FILE EMBASE
          1   FILE ESBIOBASE
          2   FILE FROSTI
          2   FILE MEDLINE
  52 FILES SEARCHED...
          2   FILE SCISEARCH
          5   FILE TOXCENTER
          5   FILE USPATFULL
          1   FILE WPIDS
          1   FILE WPINDEX

  15 FILES HAVE ONE OR MORE ANSWERS,    67 FILES SEARCHED IN STNINDEX
```

L1 QUE (SARCOIDIO? OR FIBRO?(3A)LUNG) AND RESVERATROL?

	ENTRY	SESSION
FULL ESTIMATED COST	3.85	4.06

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FILE 'WPIDS' ENTERED AT 14:44:42 ON 08 OCT 2003
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FILE 'WPINDEX' ACCESS NOT AUTHORIZED

=> s l1
L2 30 L1

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3 14 DUP REM L2 (16 DUPLICATES REMOVED)

=> d l3 abs ibib kwic 1-14

L3 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN
AB The invention is concerned with the use of lycopene, optionally in combination with vitamin E and/or C or other biol. active ingredients as

disclosed in the specification, in the manuf. of a compn. for the primary and secondary prevention of angiogenesis-assocd. pathologies and coadjuvant treatment thereof, as well as with particular novel formulations comprising lycopene. A tablet for the coadjuvant treatment of prostate carcinoma is formulated to contain 5 mg of lycopene, 200 mg of vitamin E, 250 mg of vitamin C, 37.5 mg of **resveratrol**, and 50 mg of quercetin. The daily dosage is two such tablets.

ACCESSION NUMBER: 2003:656555 CAPLUS
DOCUMENT NUMBER: 139:202483
TITLE: Compositions comprising lycopene for the treatment and prevention of angiogenesis associated pathologies
INVENTOR(S): Barella, Luca; Goralczyk, Regina; Jung, Klaus; Lein, Michael; Siler, Ulrich; Stoecklin, Elisabeth; Wertz, Karin
PATENT ASSIGNEE(S): Roche Vitamins A.-G., Switz.; Humboldt Universitaet
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068202	A1	20030821	WO 2003-EP1149	20030206

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2002-3544 A 20020215
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The invention is concerned with the use of lycopene, optionally in combination with vitamin E and/or C or other biol. active ingredients as disclosed in the specification, in the manuf. of a compn. for the primary and secondary prevention of angiogenesis-assocd. pathologies and coadjuvant treatment thereof, as well as with particular novel formulations comprising lycopene. A tablet for the coadjuvant treatment of prostate carcinoma is formulated to contain 5 mg of lycopene, 200 mg of vitamin E, 250 mg of vitamin C, 37.5 mg of **resveratrol**, and 50 mg of quercetin. The daily dosage is two such tablets.

IT **Lung**, disease
(**fibrosis**, interstitial; compns. comprising lycopene for treatment and prevention of angiogenesis assocd. pathologies)

IT 50-14-6, Vitamin D2 50-81-7, Vitamin c, biological studies 57-06-7, Allyl isothiocyanate 57-87-4, Ergosterol 67-97-0, Vitamin D3 68-26-8, all-Trans-Retinol 79-81-2, Retinyl palmitate 117-39-5, Quercetin 127-40-2, Lutein 127-47-9, Retinyl acetate 144-68-3, Zeaxanthin 446-72-0, Genistein 446-72-0D, Genistein, aglycons 458-37-7, Curcumin 472-61-7, Astaxanthin 472-70-8, .beta.-Cryptoxanthin 491-70-3, Luteolin 499-30-9, Gluconasturtiin 499-37-6 501-36-0, **Resveratrol** 502-65-8, Lycopene

505-44-2, 3-Methylsulfinylpropyl isothiocyanate 520-36-5, Apigenin 528-48-3, Fisetin 529-44-2, Myricetin 554-88-1, (Glucoiberin) 646-23-1, 5-Methylsulfinyl-pentyl isothiocyanate 700-06-1, 1H-Indole-3-methanol 961-29-5, Isoliquiritigenin 989-51-5, (-)-Epigallocatechin gallate 1257-08-5 1406-18-4, Vitamin E 2257-09-2, Phenylethyl isothiocyanate 3386-97-8, 3-Butenyl isothiocyanate 3650-09-7, Carnosic acid 3952-98-5, (Sinigrin 4356-52-9, (Glucobrassicin 4430-35-7 4478-93-7, (Sulforaphane 5041-81-6, Isoliquiritin 5187-84-8, (Neoglucobrassicin 5957-80-2, Carnosol 7235-40-7, .beta.-Carotene 12772-57-5, Radicicol 19041-09-9, Gluconapin 19356-17-3, 25-Hydroxyvitamin D3 19683-98-8, Ovalicin 21414-41-5, Glucoraphanin 21973-60-4, 8-Methylsulfinyloctyl glucosinolate 22888-70-6, Silybin 23110-15-8, Fumagillin 29782-68-1, Silydianin 32222-06-3, 1.alpha.,25-Dihydroxy-vitamin D3 33049-17-1, 6-Methylsulfinylhexyl glucosinolate 33889-69-9, Silychristin) 56142-94-0 65666-07-1, Silymarin 67884-10-0 67920-64-3, 9-Methylsulfinylnonyl glucosinolate 72581-71-6, Isosilybin 75272-81-0 75272-82-1 75272-83-2 77012-75-0, Indol-3-ylmethylisothiocyanate 83327-20-2, 4-Hydroxy glucobrassicin 83327-21-3, 4-Methoxy glucobrassicin 90996-54-6, Rhizoxin 112572-51-7, 7-Methylsulfinylheptyl glucosinolate 126463-64-7, Dihydroeponemycin 126509-46-4, Eponemycin 126769-93-5 129244-98-0 133343-34-7, Lactacystin 134381-21-8, Epoxomicin 135819-69-1 139508-73-9, Depudecin 148717-90-2, Squalamine 206443-55-2 211569-34-5, Motuporamine C 443340-10-1, 2-Methylsulfinylethyl glucosinolate 582304-76-5 582304-79-8 582304-81-2 582304-82-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising lycopene for treatment and prevention of angiogenesis assocd. pathologies)

L3 ANSWER 2 OF 14 USPATFULL on STN

AB Microcompetition for GABP between a foreign polynucleotide and cellular GABP regulated genes is a risk factor associated with many chronic diseases such as obesity, cancer, atherosclerosis, stroke, osteoarthritis, diabetes, asthma, and other autoimmune diseases. The invention uses this novel discovery to present assays for the diagnosis of these chronic diseases. The assays are based on measuring the cellular copy number of the foreign polynucleotide, measuring the rate of complex formation between GABP and either the foreign polynucleotide, or a cellular GABP regulated gene, identifying modified expression of a cellular GABP regulated gene, or identifying modified activity of the gene product of a GABP regulated gene. The invention also presents other foreign polynucleotide-type assays.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2003:152692 USPATFULL
TITLE: Diagnosis methods based on microcompetition for a limiting GABP complex
INVENTOR(S): Polansky, Hanan, Rochester, NY, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003104358	A1	20030605
APPLICATION INFO.:	US 2002-219649	A1	20020815 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2000-732360, filed on 7 Dec 2000, PENDING
DOCUMENT TYPE: Utility

09/694,108

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Hanan Polansky, 3159 S. Winton Rd., Rochester, NY, 14623
NUMBER OF CLAIMS: 32
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 28 Drawing Page(s)
LINE COUNT: 14430
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD [1035] A clone of SV40 transformed WI-38 human **lung fibroblasts**. The mRNA of the .alpha.2(I) chain was absent in the SV40 transformed WI-38 fibroblasts, whereas the mRNA of the .alpha.1(I). . .

DETD . . . hand, mainly synthesize .alpha.1(I) trimer (Moro 1977.sup.213). A high concentration of trimer was also found in SV40 transformed WI-38 human **lung fibroblasts** (Parker 1992.sup.214). Microcompetition mainly decreases the expression of the .alpha.2(I) chain (see Allebach 1985 and Parker 1989 above). Consequently, the. . .

DETD . . . the effect of ETS phosphorylation on TF transcription. The next section presents two ERK agents, all-trans retinoic acid (ATRA) and **resveratrol**, which have no effect on NF-.kappa.B, Ap1 and Sp1. As ERK agents, ATRA and **resveratrol** phosphorylate the ETS related factor(s), stimulate the binding of p300, and, therefore, should repress TF transcription.

DETD [1227] (ii) **Resveratrol** (RSVL)

DETD [1228] Confluent monolayers of human umbilical vein endothelial cells (HUVEC) were treated with **resveratrol** (100 .mu.mol/L) for 2 hours. Following **resveratrol** treatment, the cells were stimulated for 6 hours with LPS, TNF.alpha., IL-1.beta., or PMA. The results showed that **resveratrol** markedly suppressed LPS-, TNF.alpha.-, IL-1.beta.-, and PMA-induced TF activity (Pendurthi 1999.sup.257, FIG. 1A). The inhibition varied from 60% to more than 90%. HUVEC monolayers were also treated with different concentrations of **resveratrol** (0 to 200 .mu.mol/L) for 2 hours. Following **resveratrol** treatment, the cells were stimulated with TNF.alpha., IL-1.beta., or PMA. The data showed that **resveratrol** inhibited the induction of TF expression in a dose-dependent manner. To test the effect of **resveratrol** in monocytes, mononuclear cell fractions were treated with various concentrations of **resveratrol** (0 to 100 .mu.mol/L) for 2 hours and then stimulated with LPS (100 ng/mL) for 5 hours. The results showed that **resveratrol** inhibited LPS-induced TF expression in monocytes in a dose-dependent manner (Ibid, FIG. 2). To test the effect of **resveratrol** on TF mRNA, HUVEC monolayers were treated with various concentrations of **resveratrol** (0, 5, 20, 100, and 200 .mu.mol/L) for 2 hours, and then stimulated with LPS, TNF.alpha., IL-1.beta., or PMA for 2 hours. **Resveratrol** treatment reduced TF transcription in a dose-dependent manner. However, the reduced transcription was not due to diminished binding of c-Fos/c-Jun or c-Rel/p65 to the TF promoter. **Resveratrol** did not significantly change the binding of c-Fos/c-Jun to the AP-1 sites. **Resveratrol** treatment had no significant effect on binding activity to the AP-1 site in either unstimulated or LPS-, TNF.alpha.-, IL-1.beta.-, or PMA-stimulated endothelial cells (Ibid, FIG. 7). **Resveratrol** also did not significantly change the binding of NF-.kappa.B to the TF promoter. Unstimulated cells showed little binding of NF-.kappa.B,. . . LPS, TNF.alpha., IL-1.beta., or PMA induced formation of a prominent DNA-protein complex on the NF-.kappa.B site.

Preincubation of cells with **resveratrol** (100 .mu.mol/L), for 2 hours, had no effect on formation of the NF-.kappa.B DNA-protein complex (Ibid, FIG. 8).

DETD [1229] Both ATRA and **resveratrol** are ERK agents and, therefore, phosphorylate the ETS related factor(s). In general, phosphorylation of ETS related factor(s) stimulates binding of. . .

DETD . . . gene expression in human monocytes. Blood. 1998 Apr 15; 91(8): 2857-65.

.sup.257 Pendurthi U R, Williams J T, Rao L V. **Resveratrol**, a polyphenolic compound found in wine, inhibits

tissue factor expression in vascular cells: A possible mechanism for the cardiovascular benefits associated

with. . .

L3 ANSWER 3 OF 14 USPATFULL on STN

AB Cellular microcompetition for the transcription factor human GA binding protein (GABP) is a risk factor associated with obesity and obesity-related diseases such as osteoarthritis, atherosclerosis, obstructive sleep apnea, various cancers, and periodontitis. The invention uses this novel discovery to develop assays which determine the level of microcompetition in a cell. Other assays developed from the knowledge that microcompetition is occurring in cells are also disclosed. This novel discovery led to the development of assays which can determine the level of microcompetition in a cell and to select compounds to target this microcompetition syndrome. In addition, methods to treat a patient for microcompetition based disease are taught.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2003:134514 USPATFULL		
TITLE:	Microcompetition and human disease		
INVENTOR(S):	Polansky, Hanan, Rochester, NY, UNITED STATES		

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003092601	A1	20030515
APPLICATION INFO.:	US 2000-732360	A1	20001207 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-169518P	19991207 (60)
	US 2000-183184P	20000217 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	Brown, Pinnisi and Michaels, P.C., 400 M&T Bank Building-118 North Tioga Street, Ithaca, NY, 14850-4343
NUMBER OF CLAIMS:	50
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	8 Drawing Page(s)
LINE COUNT:	7921

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD [0044] WI-38 human **lung fibroblasts** were transformed by a clone of SV40. The mRNA of the .alpha.2(I) chain was absent in the SV40 transformed WI-38. . .

DETD . . . mainly synthesize a .alpha.1(I) trimer (Moro 1977.sup.5) A high concentration of trimers was also found in SV40 transformed WI-38 human **lung fibroblasts** (Parker 1992.sup.6). Microcompetition mainly decreases the expression of the .alpha.2(I) chain (see Allebach 1985 and Parker 1989 above). The relative. . .

DETD . . . effect of ETS phosphorylation on TF transcription. The next section presents two GABP kinase agent, all-trans retinoic acid (ATRA) and **resveratrol**, which have no effect on NF-.kappa.B, Ap1 and Sp1. As GABP kinase agent, ATRA and **resveratrol** phosphorylate the ETS related factor(s), stimulate the binding of p300, and, therefore, should repress TF transcription.

DETD [0211] Consider the effect of **resveratrol** (RSVL). Confluent monolayers of human umbilical vein endothelial cells (HUVEC) were treated with **resveratrol** (100 .mu.mol/L) for 2 hours. Following **resveratrol** treatment, the cells were stimulated for 6 hours with LPS, TNF.alpha., IL-1.beta. or PMA. The results showed that **resveratrol** markedly suppressed LPS-, TNF.alpha.-, IL-1.beta.-, and PMA-induced TF activity (Pendurthi 1999.sup.109, FIG. 1A). The inhibition varied from 60% to more than 90%. HUVEC monolayers were also treated with different concentrations of **resveratrol** (0 to 200 .mu.mol/L) for 2 hours. Following **resveratrol** treatment, the cells were stimulated with TNF.alpha., IL-1.beta., or PMA. The data showed that **resveratrol** inhibited the induction of TF expression in a dose-dependent manner. To test the effect of **resveratrol** in monocytes, mononuclear cell fractions were treated with various concentrations of **resveratrol** (0 to 100 .mu.mol/L) for 2 hours, and then stimulated with LPS (100 ng/mL) for 5 hours. The results showed that **resveratrol** inhibited LPS-induced TF expression in monocytes in a dose-dependent manner (Ibid, FIG. 2). To test the effect of **resveratrol** on TF mRNA, HUVEC monolayers were treated with various concentrations of **resveratrol** (0, 5, 20, 100, and 200 .mu.mol/L) for 2 hours, and then stimulated with LPS, TNF.alpha., IL-1.beta., or PMA for 2 hours. **Resveratrol** treatment reduced TF transcription in a dose-dependent manner. However, the reduced transcription was not due to diminished binding of c-Fos/c-Jun or c-Rel/p65 to the TF promoter. **Resveratrol** did not significantly change the binding of c-Fos/c-Jun to the AP-1 sites. **Resveratrol** treatment had no significant effect on binding activity to the AP-1 site in either unstimulated or LPS-, TNF.alpha.-, IL-1.beta.-, or PMA-stimulated endothelial cells (Ibid, FIG. 7). **Resveratrol** also did not significantly changes the binding of NF-.kappa.B to the TF promoter. Unstimulated cells showed little binding of NF-.kappa.B,. . . LPS, TNF.alpha., IL-1.beta., or PMA induced formation of a prominent DNA-protein complex on the NF-.kappa.B site. Preincubation of cells with **resveratrol** (100 .mu.mol/L) for 2 hours had no effect on formation of the NF-.kappa.B DNA-protein complex (Ibid, FIG. 8).

DETD [0212] Both ATRA and **resveratrol** are GABP kinase agent and, therefore, phosphorylate the ETS related factor(s). In general, phosphorylation of ETS related factor(s) stimulates binding. . .

DETD [0792] .sup.109Pendurthi U R, Williams J T, Rao L V. **Resveratrol**, a polyphenolic compound found in wine, inhibits tissue factor expression in vascular cells: A possible mechanism for the cardiovascular benefits. . .

L3 ANSWER 4 OF 14 USPATFULL on STN

AB Microcompetition for GABP between a foreign polynucleotide and a cellular GABP regulated gene is a risk factor associated with chronic disease such as obesity, cancer, atherosclerosis, stroke, osteoarthritis, diabetes, asthma, and other autoimmune diseases. The invention uses this novel discovery to present methods for the treatment of these chronic diseases. The methods are based on modifying such microcompetition, or the effect of such microcompetition on the cell.

For instance, treatment may modify the cellular copy number of the foreign polynucleotide, change the rate of complex formation between GABP and either the foreign polynucleotide or the cellular GABP regulated gene, vary the expression of the cellular GABP regulated gene, or manipulate the activity of the gene product of the cellular GABP regulated gene. The invention also presents methods for treatment of chronic diseases resulting from other foreign polynucleotide-type disruptions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2003:100088 USPATFULL
TITLE:	Treatment methods based on microcompetition for a limiting GABP complex
INVENTOR(S):	Polansky, Hanan, Rochester, NY, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003069199	A1	20030410
APPLICATION INFO.:	US 2002-219334	A1	20020815 (10)

RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2000-732360, filed on 7 Dec 2000, PENDING
DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	Hanan Polansky, 3159 S. Winton Rd., Rochester, NY, 14623
NUMBER OF CLAIMS:	26
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	28 Drawing Page(s)
LINE COUNT:	14837

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD [1068] A clone of SV40 transformed WI-38 human **lung fibroblasts**. The mRNA of the a2(I) chain was absent in the SV40 transformed WI-38 fibroblasts, whereas the mRNA of the .alpha.1(I). . .

DETD . . . mainly synthesize a .alpha.1(I) trimer (Moro 1977.sup.213). A high concentration of trimer was also found in SV40 transformed WI-38 human **lung fibroblasts** (Parker 1992.sup.214). Microcompetition mainly decreases the expression of the .alpha.2(I) chain (see Allebach 1985 and Parker 1989 above). Consequently, the. . .

DETD . . . the effect of ETS phosphorylation on TF transcription. The next section presents two ERK agents, all-trans retinoic acid (ATRA) and **resveratrol**, which have no effect on NF-.kappa.B, Ap1 and Sp1. As ERK agents, ATRA and **resveratrol** phosphorylate the ETS related factor(s), stimulate the binding of p300, and, therefore, should repress TF transcription.

DETD [1259] (ii) **Resveratrol** (RSVL)

DETD [1260] Confluent monolayers of human umbilical vein endothelial cells (HUVEC) were treated with **resveratrol** (100 .mu.mol/L) for 2 hours. Following **resveratrol** treatment, the cells were stimulated for 6 hours with LPS, TNF.alpha., IL-1.beta., or PMA. The results showed that **resveratrol** markedly suppressed LPS-, TNF.alpha.-, IL-1.beta.-, and PMA-induced TF activity (Pendurthi 1999.sup.257, FIG. 1A). The inhibition varied from 60% to more than 90%. HUVEC monolayers were also treated with different concentrations of **resveratrol** (0 to 200 .mu.mol/L) for 2 hours. Following **resveratrol** treatment, the cells were stimulated with TNF.alpha., IL-1.beta., or PMA. The data showed that **resveratrol**

inhibited the induction of TF expression in a dose-dependent manner. To test the effect of **resveratrol** in monocytes, mononuclear cell fractions were treated with various concentrations of **resveratrol** (0 to 100 .mu.mol/L) for 2 hours and then stimulated with LPS (100 ng/mL) for 5 hours. The results showed that **resveratrol** inhibited LPS-induced TF expression in monocytes in a dose-dependent manner (Ibid, FIG. 2). To test the effect of **resveratrol** on TF mRNA, HUVEC monolayers were treated with various concentrations of **resveratrol** (0, 5, 20, 100, and 200 .mu.mol/L) for 2 hours, and then stimulated with LPS, TNF.alpha., IL-1.beta., or PMA for 2 hours. **Resveratrol** treatment reduced TF transcription in a dose-dependent manner. However, the reduced transcription was not due to diminished binding of c-Fos/c-Jun or c-Rel/p65 to the TF promoter. **Resveratrol** did not significantly change the binding of c-Fos/c-Jun to the AP-1 sites. **Resveratrol** treatment had no significant effect on binding activity to the AP-1 site in either unstimulated or LPS-, TNF.alpha.-, IL-1.beta.-, or PMA-stimulated endothelial cells (Ibid, FIG. 7). **Resveratrol** also did not significantly change the binding of NF-.kappa.B to the TF promoter. Unstimulated cells showed little binding of NF-.kappa.B,. . . LPS, TNF.alpha., IL-1.beta., or PMA induced formation of a prominent DNA-protein complex on the NF-.kappa.B site. Preincubation of cells with **resveratrol** (100 .mu.mol/L), for 2 hours, had no effect on formation of the NF-.kappa.B DNA-protein complex (Ibid, FIG. 8).

DETD [1261] Both ATRA and **resveratrol** are ERK agents and, therefore, phosphorylate the ETS related factor(s). In general, phosphorylation of ETS related factor(s) stimulates binding of. . .

DETD [2374] .sup.257 Pendurthi U R, Williams J T, Rao L V. **Resveratrol**, a polyphenolic compound found in wine, inhibits tissue factor expression in vascular cells: A possible mechanism for the cardiovascular benefits. . .

L3 ANSWER 5 OF 14 USPATFULL on STN

AB A recent discovery showed that microcompetition for GABP between a foreign polynucleotide and a cellular GABP regulated gene is a risk factor for some of the major chronic diseases, such as obesity, cancer, atherosclerosis, stroke, osteoarthritis, diabetes, asthma, and other autoimmune diseases. The invention uses this novel discovery to present assays for screening compounds based on their effectiveness in modulating such microcompetition, or the effects of such microcompetition on the cell. The selected compounds can be used in treatment of these chronic diseases. The invention also presents assays for screening compounds that can be used in treatment of chronic diseases resulting from other foreign polynucleotide-type disruptions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2003:99511 USPATFULL
TITLE:	Drug discovery assays based on microcompetition for a limiting GABP complex
INVENTOR(S):	Polansky, Hanan, Rochester, NY, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003068616	A1	20030410
APPLICATION INFO.:	US 2002-223050	A1	20020814 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2000-732360, filed on 7 Dec 2000, PENDING		

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Hanan Polansky, 3159 S. Winton Rd., Rochester, NY, 14623
NUMBER OF CLAIMS: 55
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 28 Drawing Page(s)
LINE COUNT: 14981
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD [1040] A clone of SV40 transformed WI-38 human **lung fibroblasts**. The mRNA of the .alpha.2(I) chain was absent in the SV40 transformed WI-38 fibroblasts, whereas the mRNA of the .alpha.1(I). . .

DETD . . . mainly synthesize a .alpha.1(I) trimer (Moro 1977.sup.213). A high concentration of trimer was also found in SV40 transformed WI-38 human **lung fibroblasts** (Parker 1992.sup.214). Microcompetition mainly decreases the expression of the .alpha.2(I) chain (see Allebach 1985 and Parker 1989 above). Consequently, the. . .

DETD . . . the effect of ETS phosphorylation on TF transcription. The next section presents two ERK agents, all-trans retinoic acid (ATRA) and **resveratrol**, which have no effect on NF-.kappa.B, Ap1 and Sp1. As ERK agents, ATRA and **resveratrol** phosphorylate the ETS related factor(s), stimulate the binding of p300, and, therefore, should repress TF transcription.

DETD [1236] (ii) **Resveratrol** (RSVL)

DETD [1237] Confluent monolayers of human umbilical vein endothelial cells (HUVEC) were treated with **resveratrol** (100 .mu.mol/L) for 2 hours. Following **resveratrol** treatment, the cells were stimulated for 6 hours with LPS, TNF.alpha., IL-1.beta., or PMA. The results showed that **resveratrol** markedly suppressed LPS-, TNF.alpha.-, IL-1.beta.-, and PMA-induced TF activity (Pendurthi 1999.sup.257, FIG. 1A). The inhibition varied from 60% to more than 90%. HUVEC monolayers were also treated with different concentrations of **resveratrol** (0 to 200 .mu.mol/L) for 2 hours. Following **resveratrol** treatment, the cells were stimulated with TNF.alpha., IL-1.beta., or PMA. The data showed that **resveratrol** inhibited the induction of TF expression in a dose-dependent manner. To test the effect of **resveratrol** in monocytes, mononuclear cell fractions were treated with various concentrations of **resveratrol** (0 to 100 .mu.mol/L) for 2 hours and then stimulated with LPS (100 ng/mL) for 5 hours. The results showed that **resveratrol** inhibited LPS-induced TF expression in monocytes in a dose-dependent manner (Ibid, FIG. 2). To test the effect of **resveratrol** on TF mRNA, HUVEC monolayers were treated with various concentrations of **resveratrol** (0, 5, 20, 100, and 200 .mu.mol/L) for 2 hours, and then stimulated with LPS, TNF.alpha., IL-1.beta., or PMA for 2 hours. **Resveratrol** treatment reduced TF transcription in a dose-dependent manner. However, the reduced transcription was not due to diminished binding of c-Fos/c-Jun or c-Rel/p65 to the TF promoter. **Resveratrol** did not significantly change the binding of c-Fos/c-Jun to the AP-1 sites. **Resveratrol** treatment had no significant effect on binding activity to the AP-1 site in either unstimulated or LPS-, TNF.alpha.-, IL-1.beta.-, or PMA-stimulated endothelial cells (Ibid, FIG. 7). **Resveratrol** also did not significantly change the binding of NF-.kappa.B to the TF promoter. Unstimulated cells showed little binding of NF-.kappa.B,. . . LPS, TNF.alpha., IL-1.beta., or PMA induced

formation of a prominent DNA-protein complex on the NF-.kappa.B site. Preincubation of cells with **resveratrol** (100 .mu.mol/L), for 2 hours, had no effect on formation of the NF-.kappa.B DNA-protein complex (Ibid, FIG. 8).

DETD [1238] Both ATRA and **resveratrol** are ERK agents and, therefore, phosphorylate the ETS related factor(s). In general, phosphorylation of ETS related factor(s) stimulates binding of. . .

DETD [2354] .sup.257 Pendurthi U R, Williams J T, Rao L V. **Resveratrol**, a polyphenolic compound found in wine, inhibits tissue factor expression in vascular cells: A possible mechanism for the cardiovascular benefits. . .

L3 ANSWER 6 OF 14 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 1

AB The methanol extracts of nine medicinal plants traditionally used in Chinese medicine were screened for antioxidant activity versus **resveratrol**, which has been shown to protect cells from oxidative damage (Toxicol. Lett. 102 (1998) 5). Most of the plant extracts used in this study inhibited the H2O2-induced apoptosis of Chinese hamster **lung fibroblast** (V79-4) cells. The extracts of Areca catechu var. dulcissima, Paeonia suffruticosa, Alpinia officinarum, Glycyrrhiza uralensis and Cinnamomun cassia strongly enhanced viability against H2O2-induced oxidative damage in V79-4 cells. Relatively high levels of 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity were detected in extracts of Areca catechu var. dulcissima, Paeonia suffruticosa and Cinnamomun cassia (IC50<6.0 mug/ml). The activities of superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX) were dose-dependently enhanced in V79-4 cells treated with most of the plant extracts. The extracts of Areca catechu var. dulcissima showed higher antioxidant activity than **resveratrol** in all experiments. These results suggest that the plant extracts prevent oxidative damage in normal cells probably because of their antioxidant characteristics.

ACCESSION NUMBER: 2003:257489 BIOSIS
DOCUMENT NUMBER: PREV200300257489
TITLE: Screening of medicinal plant extracts for antioxidant activity.
AUTHOR(S): Lee, Si Eun; Hwang, Hyun Jin; Ha, Jung-Sun; Jeong, Han-Seung; Kim, Jeong Hee (1)
CORPORATE SOURCE: (1) Department of Biochemistry, College of Dentistry, Kyung Hee University, 1 Hoegi-Dong, Dongdaemoon-Ku, Seoul, 130-701, South Korea: jhkimh@khu.ac.kr South Korea
SOURCE: Life Sciences, (May 30 2003) Vol. 73, No. 2, pp. 167-179. print.
ISSN: 0024-3205.
DOCUMENT TYPE: Article
LANGUAGE: English

AB The methanol extracts of nine medicinal plants traditionally used in Chinese medicine were screened for antioxidant activity versus **resveratrol**, which has been shown to protect cells from oxidative damage (Toxicol. Lett. 102 (1998) 5). Most of the plant extracts used in this study inhibited the H2O2-induced apoptosis of Chinese hamster **lung fibroblast** (V79-4) cells. The extracts of Areca catechu var. dulcissima, Paeonia suffruticosa, Alpinia officinarum, Glycyrrhiza uralensis and Cinnamomun cassia strongly enhanced. . . cells treated with most of the plant extracts. The extracts of Areca catechu var. dulcissima showed higher antioxidant activity than **resveratrol** in all experiments. These results suggest that the plant extracts prevent oxidative damage in normal cells probably because

of their. . .
IT . . .
radical scavenging activity; catalase [EC 1.11.1.6]; glutathione peroxidase [EC 1.11.1.9, GPX]; hydrogen peroxide; medicinal plant methanol extracts: antioxidant activity, pharmaceutical; **resveratrol**: pharmaceutical; superoxide dismutase [EC 1.15.1.1, SOD]
ORGN . . .
suffruticosa (Paeoniaceae): medicinal plant; Solvia miltiorrhiza (Labiatae): medicinal plant; Spirodela polyrrhiza (Lemnaceae): medicinal plant; V79-4 cell line (Cricetidae): Chinese hamster **lung fibroblast** cells
ORGN Organism Superterms
Angiosperms; Animals; Chordates; Dicots; Mammals; Monocots; Nonhuman Mammals; Nonhuman Vertebrates; Plants; Rodents; Spermatophytes; Vascular Plants; Vertebrates
RN 1898-66-4 (1,1-DIPHENYL-2-PICRYLHYDRAZYL)
9001-05-2 (CATALASE)
9001-05-2 (EC 1.11.1.6)
9013-66-5 (GLUTATHIONE PEROXIDASE)
9013-66-5 (EC 1.11.1.9)
7722-84-1 (HYDROGEN PEROXIDE)
501-36-0 (**RESVERATROL**)
9054-89-1 (SUPEROXIDE DISMUTASE)
9054-89-1 (EC 1.15.1.1)

L3 ANSWER 7 OF 14 FROSTI COPYRIGHT 2003 LFRA on STN
AN 584005 FROSTI
AB A composition comprising **resveratrol** and its analogue is useful in the treatment of inflammatory respiratory disorders such as bronchitis, asthma, cystic **fibrosis**, bronchiectasis and interstitial **lung** diseases. It can be given by oral or pulmonary administration and is claimed to be more effective than oral, parenteral or pulmonary administration of corticosteroids. **Resveratrol** has known activity in as a cancer chemopreventive agent.
TITLE: Administration of **resveratrol** to treat inflammatory respiratory disorders.
INVENTOR: Donnelly L.E.; ~~Barnes~~ P.J.
PATENT ASSIGNEE: Imperial College Innovations Ltd
SOURCE: PCT Patent Application
PATENT INFORMATION: WO 2002032410 ~~A2~~ 20020425
APPLICATION INFORMATION: 20011019
PRIORITY INFORMATION: United States 20001019
NOTE: 20020425
DOCUMENT TYPE: Patent
LANGUAGE: English
SUMMARY LANGUAGE: English
TI Administration of **resveratrol** to treat inflammatory respiratory disorders.
AB A composition comprising **resveratrol** and its analogue is useful in the treatment of inflammatory respiratory disorders such as bronchitis, asthma, cystic **fibrosis**, bronchiectasis and interstitial **lung** diseases. It can be given by oral or pulmonary administration and is claimed to be more effective than oral, parenteral or pulmonary administration of corticosteroids. **Resveratrol** has known activity in as a cancer chemopreventive agent.

Appl.

CT FUNCTIONAL FOODS; HEALTH; INFLAMMATORY RESPIRATORY DISORDERS; PATENT; PCT PATENT; RESPIRATORY DISORDERS; **RESVERATROL**

L3 ANSWER 8 OF 14 USPATFULL on STN

AB Osteoarthritis is treated by a composition containing both apocynin and an inhibitor of inducible nitric oxide synthase such as curcumin. Further components such as boswellic acids, glucosamine, acetylcysteine and boron further enhance the beneficial effect of apocynin and curcumin.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2002:326052 USPATFULL		
TITLE:	Composition for the treatment of osteoarthritis		
INVENTOR(S):	Graus, Ivo Maria Franciscus, Wg Ede, NETHERLANDS Smit, Hobbe Friso, As Utrecht, NETHERLANDS		
PATENT ASSIGNEE(S):	N.V. Nutricia, Zoetermeer, NETHERLANDS (non-U.S. corporation)		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6492429	B1	20021210
APPLICATION INFO.:	US 2000-662123		20000914 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2000-613562, filed on 10 Jul 2000		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Tate, Christopher R.		
ASSISTANT EXAMINER:	Patten, Patricia A		
LEGAL REPRESENTATIVE:	Browdy and Neimark, P.L.L.C.		
NUMBER OF CLAIMS:	8		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)		
LINE COUNT:	298		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . anti-inflammatory, anti-arthritic and anti-ulcerogenic activities. WO 97/07796 claims the use of boswellic acid for the treatment of diseases, such as **lung** emphysema, cystic **fibrosis**, rheumatoid arthritis etc, which are induced by leucocytic elastase or plasmin activity.

SUMM . . . group, preferably a dihydroxybenzopyran group, were found to be useful in this respect. Examples of suitable phenolic compounds include curcuminoids, **resveratrol**, quercetin and other hydroxyflavones, catechins such as epicatechin, catechin, gallocatechin, afzelechin, epigallocatechin gallate, epicatechin gallate, compounds having activated phenolic groups. . .

DETD . . . Glucosamine sulfate (potassium) 1500 mg
Chondroitin sulfate 1200 mg
Picrorhiza kurrooa extract (10% apocynin) 20 mg
Rosemary extract 250 mg
Resveratrol (grape skin extract) 500 .mu.g
Urtica dioica extract 750 mg

L3 ANSWER 9 OF 14 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 2002-454579 [48] WPIDS

AB WO 200232410 A UPAB: 20020730
NOVELTY - A novel method for treating a patient suffering from or predisposed to developing an inflammatory respiratory disorder comprises administering to the patient a pharmaceutical formulation that comprises a

carrier and an active agent selected from **resveratrol**, salts, esters, amides, prodrugs, and analogs or combinations.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a pharmaceutical formulation for treatment of an inflammatory respiratory disorder, comprising a first active agent selected from **resveratrol**, salts, esters, amides, prodrugs, and analogs or combinations, and a second active agent selected from glucocorticoids, non-steroidal antiinflammatory drugs, macrolide antibiotics, bronchodilators and combinations; and

(2) a pharmaceutical formulation for pulmonary administration, comprising an active agent selected from **resveratrol**, its salts, esters, amides, prodrugs or analogs, and a carrier suitable for pulmonary drug administration.

ACTIVITY - Antiinflammatory; antiasthmatic; antiallergic; cytostatic; immunosuppressive; anti-HIV.

MECHANISM OF ACTION - **Resveratrol** inhibits cyclooxygenase (COX) activity; inhibitor of inducible NO synthase (iNOS) expression; inhibitor of inflammatory gene expression. The expression of inflammatory genes was evaluated in cells transformed with luciferase reporter genes containing sites for transcription factors (Tf). The A549 cells were stably transfected by routine methods with luciferase reporters containing the transcription factors NF-kappaB, TRE (AP-1, TPA responsive element) and CRE (cAMP responsive element). Luciferase activity of cell lysates resuspended in 100 mml cell lysis buffer mixed (40 mml resuspended lysate: 40 mml assay reagent) was measured using the luciferase assay system, with emitted light measured by a luminometer. **Resveratrol** inhibited NF-kappaB dependent transcription completely with an EC50 value of 21 plus or minus 7 mu M. Dexamethasone inhibited NF-kappaB dependent transcription by only 41% with an EC50 value of 16 plus or minus 12 mu M. **Resveratrol** inhibited TRE dependent transcription by 85% with an EC50 value of 7 plus or minus 4 mu M. Dexamethasone inhibited CRE dependent transcription by 62% with an EC50 value of 3.4 plus or minus 3 mu M. **Resveratrol** inhibited CRE dependent transcription by 91% with an EC50 value of 30 plus or minus 17 mu M. Dexamethasone inhibited CRE dependent transcription by 62% with an EC50 value of 3.4 plus or minus 3 mu M. **Resveratrol** was also shown to inhibit iNOS, interleukin 8 and granulocyte macrophage-colony stimulating factor.

USE - The formulations may be used to treat asthma, atopic asthma, non-atopic asthma, chronic obstructive pulmonary disease (COPD), alveolitis or interstitial lung disease (ILD) (claimed). The formulations may be used where the disorder is a result of occupational or environmental exposure to smoke, an organic or inorganic dust, or an allergen (claimed). The organic or inorganic dust may be derived e.g. silica, asbestos, beryllium, coal, carbon, wood, starch, sugar, flour, synthetic polymers, cellulosic materials, clay, concrete, lime or earth (claimed). The formulations can be used for treating e.g. chronic bronchitis, emphysema, fibrolysing alveolitis, sarcosis, bronchiectasis, or **fibrotic lung** diseases, asbestosis, pulmonary berylliosis, coal worker's pneumoniosis, silicosis and byssinosis (cotton dust). They can be useful as a substitute for corticosteroids, e.g. in the treatment of patients exhibiting significant systemic side effects in response to corticosteroid administration, e.g. HPA regulatory endocrine insufficiency. They can also be used to treat inflammatory respiratory conditions in immunocompromised patients, e.g. immunocompromised by HIV disease. Previously it has been found that **resveratrol** acts as an antioxidant and antimutagen and induces phase II drug-metabolizing enzymes; mediates antiinflammatory effects and inhibits cyclooxygenase and hyroperoxidase; and induces human promyelocytic leukemia cell

differentiation.
Dwg.0/0

ACCESSION NUMBER: 2002-454579 [48] WPIDS
DOC. NO. CPI: C2002-129249
TITLE: Use of **resveratrol** or salts, esters, amides, prodrugs, or analogs for treating inflammatory respiratory disorder, e.g. asthma, chronic obstructive pulmonary disease, alveolitis, or interstitial lung disease.
DERWENT CLASS: B07
INVENTOR(S): ~~BARNES, P J; DONNELLY, L E~~
PATENT ASSIGNEE(S): (IMCO-N) IMPERIAL COLLEGE INNOVATIONS LTD
COUNTRY COUNT: 98
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002032410	A2	20020425	(200248)*	EN	34

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001095760	A	20020429	(200255)	
EP 1326595	A2	20030716	(200347)	EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002032410	A2	WO 2001-GB4672	20011019
AU 2001095760	A	AU 2001-95760	20011019
EP 1326595	A2	EP 2001-976492	20011019
		WO 2001-GB4672	20011019

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001095760	A	Based on	WO 2002032410
EP 1326595	A2	Based on	WO 2002032410

PRIORITY APPLN. INFO: US 2000-694108 20001019

TI Use of **resveratrol** or salts, esters, amides, prodrugs, or analogs for treating inflammatory respiratory disorder, e.g. asthma, chronic obstructive pulmonary disease, alveolitis, or. . .

AB . . .
respiratory disorder comprises administering to the patient a pharmaceutical formulation that comprises a carrier and an active agent selected from **resveratrol**, salts, esters, amides, prodrugs, and analogs or combinations.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a pharmaceutical formulation for treatment of an inflammatory respiratory disorder, comprising a first active agent selected from **resveratrol**, salts, esters, amides, prodrugs, and analogs or

combinations, and a second active agent selected from glucocorticoids, non-steroidal antiinflammatory drugs, macrolide antibiotics, bronchodilators and combinations; and

(2) a pharmaceutical formulation for pulmonary administration, comprising an active agent selected from **resveratrol**, its salts, esters, amides, prodrugs or analogs, and a carrier suitable for pulmonary drug administration.

ACTIVITY - Antiinflammatory; antiasthmatic; antiallergic; cytostatic; immunosuppressive; anti-HIV.

MECHANISM OF ACTION - **Resveratrol** inhibits cyclooxygenase (COX) activity; inhibitor of inducible NO synthase (iNOS) expression; inhibitor of inflammatory gene expression. The expression of inflammatory. . . resuspended lysate: 40 mml assay reagent) was measured using the luciferase assay system, with emitted light measured by a luminometer. **Resveratrol** inhibited NF-kappaB dependent transcription completely with an EC50 value of 21 plus or minus 7 mu M. Dexamethasone inhibited NF-kappaB dependent transcription by only 41% with an EC50 value of 16 plus or minus 12 mu M. **Resveratrol** inhibited TRE dependent transcription by 85% with an EC50 value of 7 plus or minus 4 mu M. Dexamethasone inhibited CRE dependent transcription by 62% with an EC50 value of 3.4 plus or minus 3 mu M. **Resveratrol** inhibited CRE dependent transcription by 91% with an EC50 value of 30 plus or minus 17 mu M. Dexamethasone inhibited CRE dependent transcription by 62% with an EC50 value of 3.4 plus or minus 3 mu M. **Resveratrol** was also shown to inhibit iNOS, interleukin 8 and granulocyte macrophage-colony stimulating factor.

USE - The formulations may be. . . lime or earth (claimed). The formulations can be used for treating e.g. chronic bronchitis, emphysema, fibrolysing alveolitis, sarcosis, bronchiectasis, or **fibrotic lung** diseases, asbestosis, pulmonary berylliosis, coal worker's pneumoniosis, silicosis and byssinosis (cotton dust). They can be useful as a substitute for. . . used to treat inflammatory respiratory conditions in immunocompromised patients, e.g. immunocompromised by HIV disease. Previously it has been found that **resveratrol** acts as an antioxidant and antimutagen and induces phase II drug-metabolizing enzymes; mediates antiinflammatory effects and inhibits cyclooxygenase and hyroperoxidase;. . .

TECH UPTX: 20020730

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The **resveratrol** (3,5,4'-trihydroxystilbene) may be isolated from wine or grape skins, or it may be chemically synthesized. The active agent may be cis-**resveratrol** or trans-**resveratrol** or their salts, esters, amides, prodrugs or analogs, or a conjugate of cis-**resveratrol** or trans-**resveratrol** and a mono- or di-saccharide, particularly cis-**resveratrol** glucoside or trans-**resveratrol** glucoside.

L3 ANSWER 10 OF 14 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 2

AB We previously reported that 3,5,4'-trihydroxy-trans-stilbene (**resveratrol**), a polyphenolic phytoalexin found in grapes, induces a high frequency of sister chromatid exchanges (SCEs) in vitro. In this study, to investigate structure activity relationships, we synthesized six analogues of **resveratrol** differing in number and position of hydroxy groups, and we investigated their activity in chromosomal aberration (CA), micronucleus (MN) and sister chromatid exchange (SCE) tests in a Chinese hamster cell line (CHL). Two of the six analogues (3,4'-dihydroxy-trans-stilbene and 4-hydroxy-trans-stilbene) showed clear

positive responses in a concentration-dependent manner in all three tests. Both were equal to or stronger than **resveratrol** in genotoxicity. The 4'-hydroxy (OH) analogue had the simplest chemical structure and was the most genotoxic. The other analogues did not have a 4'-hydroxy group. These results suggested that 4'-hydroxy group is essential to the genotoxicity of stilbenes.

ACCESSION NUMBER: 2003:56197 BIOSIS
DOCUMENT NUMBER: PREV200300056197
TITLE: The 4'-hydroxy group is responsible for the in vitro cytogenetic activity of **resveratrol**.
AUTHOR(S): Matsuoka, Atsuko (1); Takeshita, Kenji; Furuta, Ayumi; Ozaki, Masayasu; Fukuhara, Kiyoshi; Miyata, Naoki
CORPORATE SOURCE: (1) Division of Medical Devices, National Institute of Health Sciences, 1-18-1 Kamiyoga, Setagaya-ku, Tokyo, 158-8501, Japan: matsuoka@nihs.go.jp Japan
SOURCE: Mutation Research, (26 November 2002) Vol. 521, No. 1-2, pp. 29-35. print.
ISSN: 0027-5107.
DOCUMENT TYPE: Article
LANGUAGE: English

TI The 4'-hydroxy group is responsible for the in vitro cytogenetic activity of **resveratrol**.

AB We previously reported that 3,5,4'-trihydroxy-trans-stilbene (**resveratrol**), a polyphenolic phytoalexin found in grapes, induces a high frequency of sister chromatid exchanges (SCEs) in vitro. In this study, to investigate structure activity relationships, we synthesized six analogues of **resveratrol** differing in number and position of hydroxy groups, and we investigated their activity in chromosomal aberration (CA), micronucleus (MN) and. . . 4-hydroxy-trans-stilbene) showed clear positive responses in a concentration-dependent manner in all three tests. Both were equal to or stronger than **resveratrol** in genotoxicity. The 4'-hydroxy (OH) analogue had the simplest chemical structure and was the most genotoxic. The other analogues did. . .

IT Major Concepts
Genetics; Toxicology

IT Chemicals & Biochemicals
3,3'-dihydroxy-trans-stilbene: genotoxin, **resveratrol** analog, toxin; 3,4'-dihydroxy-trans-stilbene: genotoxin, **resveratrol** analog, toxin; 3,5,3'-trihydroxy-trans-stilbene: genotoxin, **resveratrol** analog, toxin; 3,5-dihydroxy-trans-stilbene: genotoxin, **resveratrol** analog, toxin; 3-hydroxy-trans-stilbene: genotoxin, **resveratrol** analog, toxin; 4-hydroxy-trans-stilbene: genotoxin, **resveratrol** analog, toxin; **resveratrol** [3,5,4'-trihydroxy-trans-stilbene]: 4'-hydroxy group, cytogenetic activity, genotoxin, toxin

ORGN Super Taxa
Cricetidae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
CHL cell line (Cricetidae): Chinese hamster **lung fibroblast** cells

ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

RN 22139-77-1 (3,5-DIHYDROXY-TRANS-STILBENE)
501-36-0 (**RESVERATROL**)

L3 ANSWER 11 OF 14 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 3

AB Purpose: To explore possible antiviral properties of **resveratrol** against human cytomegalovirus (HCMV) replication. **Resveratrol** is a naturally occurring antioxidant found in grapes and red wine that has been shown to protect against coronary artery disease and inhibit platelet aggregation. Since **resveratrol** also exhibits antiviral properties against herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) replication on monolayers of Vero cells in a dose-dependent and reversible manner (Docherty et al, 1999), we hypothesized that this phytoalexin would also inhibit HCMV replication in culture. Methods: Monolayers of human embryonic **lung** (MRC-5) **fibroblasts** were inoculated with known amounts of HCMV (AD169). Following a 1 hr adsorption, **resveratrol** diluted in either 1% ethanol or 1% DMSO at concentrations of 1, 5, 10, 25, or 50 ug/ml was added to washed HCMV-infected cell monolayers. Control HCMV-infected monolayers were maintained in growth media without **resveratrol**. All monolayers were scored and compared for number and size of HCMV plaques at 10 days postinfection. Results: **Resveratrol** reduced the formation of HCMV plaques in a dose-dependent manner. Although 25 and 50 ug/ml proved to be toxic to MRC-5 cells by 10 days postinfection, **resveratrol** at a concentration of 10 ug/ml reduced HCMV plaque formation in three separate experiments by 70 to 89% (average reduction = 80%). Plaque size was also markedly reduced at this concentration. Conclusion: **Resveratrol** exhibits antiviral activity against HCMV replication in culture. When compared with results reported previously for HSV-1 and HSV-2, HCMV appears to be more sensitive to **resveratrol** than HSV-1 and HSV-2 (10 ug/ml versus 50 ug/ml, respectively).

ACCESSION NUMBER: 2003:175211 BIOSIS
DOCUMENT NUMBER: PREV200300175211
TITLE: Does **Resveratrol** Exhibit Antiviral Properties Against Cytomegalovirus Replication.
AUTHOR(S): Atreides, S. -P. A. (1); Wilkins, C. (1); Ekworomadu, C. O. (1); Docherty, J. J.; Dix, R. D. (1)
CORPORATE SOURCE: (1) Jones Eye Inst, Univ of Arkansas for Med Sci, Little Rock, AR, USA USA
SOURCE: ARVO Annual Meeting Abstract Search and Program Planner, (2002) Vol. 2002, pp. Abstract No. 4325. cd-rom. Meeting Info.: Annual Meeting of the Association For Research in Vision and Ophthalmology Fort Lauderdale, Florida, USA May 05-10, 2002
DOCUMENT TYPE: Conference
LANGUAGE: English
TI Does **Resveratrol** Exhibit Antiviral Properties Against Cytomegalovirus Replication.
AB Purpose: To explore possible antiviral properties of **resveratrol** against human cytomegalovirus (HCMV) replication. **Resveratrol** is a naturally occurring antioxidant found in grapes and red wine that has been shown to protect against coronary artery disease and inhibit platelet aggregation. Since **resveratrol** also exhibits antiviral properties against herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) replication on monolayers of Vero. . . et al, 1999), we hypothesized that this phytoalexin would also inhibit HCMV replication in culture. Methods: Monolayers of human embryonic **lung** (MRC-5) **fibroblasts** were inoculated with known amounts of HCMV (AD169). Following a 1 hr adsorption, **resveratrol** diluted in either 1% ethanol or 1% DMSO at concentrations of 1, 5, 10, 25, or 50 ug/ml was added to washed HCMV-infected cell monolayers. Control HCMV-infected monolayers were maintained in growth media without **resveratrol**. All monolayers were scored and compared for number and size of HCMV

plaques at 10 days postinfection. Results: **Resveratrol** reduced the formation of HCMV plaques in a dose-dependent manner. Although 25 and 50 ug/ml proved to be toxic to MRC-5 cells by 10 days postinfection, **resveratrol** at a concentration of 10 ug/ml reduced HCMV plaque formation in three separate experiments by 70 to 89% (average reduction = 80%). Plaque size was also markedly reduced at this concentration. Conclusion: **Resveratrol** exhibits antiviral activity against HCMV replication in culture. When compared with results reported previously for HSV-1 and HSV-2, HCMV appears to be more sensitive to **resveratrol** than HSV-1 and HSV-2 (10 ug/ml versus 50 ug/ml, respectively).

IT Major Concepts
Infection; Pharmacology

IT Chemicals & Biochemicals
DMSO: concentrations; ethanol: concentrations; **resveratrol**: antiinfective - drug, antiviral - drug, concentration, phytoalexin, toxicity

ORGN . . .
dsDNA Viruses, Viruses, Microorganisms; Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
MRC-5 cell line (Hominidae): host, human embryonic **lung fibroblasts**, monolayers; herpes simplex virus type 1 [HSV-1, Human herpesvirus 1] (Herpesviridae): pathogen; herpes simplex virus type 2 [HSV-2, Human herpesvirus. . .

RN 67-68-5 (DMSO)
64-17-5 (ETHANOL)
501-36-0 (**RESVERATROL**)

L3 ANSWER 12 OF 14 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 4

AB **Resveratrol**, a trihydroxystilbene found in grapes and other plants, has been shown to be active in inhibiting multistage carcinogenesis. Using **resveratrol** as a prototype, we have synthesized a number of polyhydroxy- and polymethoxy-stilbenes and tested their anti-proliferative effect in normal and transformed human cells. Here we show that one of the **resveratrol** analogs, 3,4,5,4'-tetrahydroxystilbene (R-4), specifically inhibited the growth of SV40 virally transformed WI38 cells (WI38VA) at 10 muM, but had no effect on normal WI38 cells at even higher concentrations. R-4 also prominently induced apoptosis in WI38VA cells, but not in WI38 cells. RNase protection assay showed that R-4 significantly induced the expression of p53, GADD45 and Bax genes and concomitantly suppressed the expression of bcl-2 gene in WI38VA, but not in WI38 cells. A large increase in p53 DNA binding activity and the presence of p53 in the Bax promoter binding complex suggested that p53 was responsible for the Bax gene expression induced by R-4 in transformed cells. Within 4 h of treatment with R-4, the Bax to bcl-2 protein ratio in WI38 and WI38VA cells was, respectively, 0.1 and 105, a difference of three orders of magnitude. While R-4 prominently induced the p53/Bax pro-apoptotic genes, it also concomitantly suppressed the expression of Cox-2 in WI38VA cells. Taken together, our study suggests that the induction of p53 gene by R-4 in transformed cells may play a key role in the differential growth inhibition and apoptosis of transformed cells.

ACCESSION NUMBER: 2001:176611 BIOSIS
DOCUMENT NUMBER: PREV200100176611
TITLE: **Resveratrol** analog, 3,4,5,4'-tetrahydroxystilbene, differentially induces pro-apoptotic p53/Bax gene expression and inhibits the growth of

transformed cells but not their normal counterparts.

AUTHOR(S): Lu, Jiebo; Ho, Chi-Tang; Ghai, Geetha; Chen, Kuang Yu (1)
CORPORATE SOURCE: (1) Department of Chemistry, Rutgers University, 610 Taylor Road, Piscataway, NJ, 08854-8087: kychen@rutchem.rutgers.edu USA
SOURCE: Carcinogenesis (Oxford), (February, 2001) Vol. 22, No. 2, pp. 321-328. print.
ISSN: 0143-3334.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

TI **Resveratrol** analog, 3,4,5,4'-tetrahydroxystilbene, differentially induces pro-apoptotic p53/Bax gene expression and inhibits the growth of transformed cells but not their normal counterparts.. . .

AB **Resveratrol**, a trihydroxystilbene found in grapes and other plants, has been shown to be active in inhibiting multistage carcinogenesis. Using **resveratrol** as a prototype, we have synthesized a number of polyhydroxy- and polymethoxy-stilbenes and tested their anti-proliferative effect in normal and transformed human cells. Here we show that one of the **resveratrol** analogs, 3,4,5,4'-tetrahydroxystilbene (R-4), specifically inhibited the growth of SV40 virally transformed WI38 cells (WI38VA) at 10 muM, but had no. . .

IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Genetics; Tumor Biology

IT Chemicals & Biochemicals
3,4,5,4'-tetrahydroxystilbene: **resveratrol** analog; Bax protein; bcl-2 protein; **resveratrol**: carcinogenesis inhibition

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
WI38 cell line (Hominidae): human **lung fibroblast** cells; WI38VA cell line (Hominidae): SV40 virally transformed, apoptosis, human **lung fibroblast** cells

ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

RN 501-36-0 (**RESVERATROL**)

L3 ANSWER 13 OF 14 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 5

AB **Resveratrol**, a natural phytoestrogen, has been reported to promote differentiation of murine MC3T3-E1 osteoblasts and to inhibit proliferation of prostate cancer cell lines. In the present study we tested the effects of **resveratrol** on the increased proliferation of human AHTO-7 osteoblastic cell line induced by conditioned media (CM) from a panel of carcinoma cell lines. This compound was found to modulate AHTO-7 proliferation in a tamoxifen-sensitive mechanism at lower concentrations, but failed to induce the osteoblast differentiation marker alkaline phosphatase (ALP) in contrast to vitamin D3. The proliferative response of AHTO-7 cells to conditioned media from carcinoma cell lines was diminished (30-71.4% inhibition) upon pretreatment with 0.5 muM **resveratrol**. Highest inhibition was demonstrated for pancreas (BxPC3, Panc-1), breast (ZR75-1) and renal (ACHN) carcinoma cell line supernatants whereas the effect on colon carcinoma (SW620, Colo320DM) cell CM and prostate cancer (PC3, DU 145 and LNCaP) CM was less pronounced. Direct addition of **resveratrol** affected only supernatants of cell lines (<25% inhibition) exhibiting growth stimulatory activity for

normal WI-38 **lung fibroblasts**. **Resveratrol** inhibited proliferation of DU145 and LNCaP cells in concentrations exceeding 5 muM, altered cell cycle distribution of all prostate cancer cell lines in concentrations as low as 0.5 muM, but did not inhibit the production of osteoblastic factors by these lines. In conclusion, **resveratrol** failed to induce ALP activity as marker of osteoblast differentiation in human osteoblastic AHTO-7 cells, however, inhibited their response to osteoblastic carcinoma-derived growth factors in concentrations significantly lower than those to reduce growth of cancer cells, thus effectively modulating tumor - osteoblast interaction.

ACCESSION NUMBER: 2000:21931 BIOSIS
DOCUMENT NUMBER: PREV200000021931
TITLE: **Resveratrol** pretreatment desensitizes AHTO-7 human osteoblasts to growth stimulation in response to carcinoma cell supernatants.
AUTHOR(S): Ulsperger, Ernst; Hamilton, Gerhard (1); Raderer, Markus; Baumgartner, Gerhard; Hejna, Michael; Hoffmann, Oskar; Mallinger, Rudolf
CORPORATE SOURCE: (1) Ludwig Boltzmann Institute of Clinical Oncology, Balderichgasse 26/13, A-1170, Vienna Austria
SOURCE: International Journal of Oncology, (Nov., 1999) Vol. 15, No. 5, pp. 955-959.
ISSN: 1019-6439.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

TI **Resveratrol** pretreatment desensitizes AHTO-7 human osteoblasts to growth stimulation in response to carcinoma cell supernatants.

AB **Resveratrol**, a natural phytoestrogen, has been reported to promote differentiation of murine MC3T3-E1 osteoblasts and to inhibit proliferation of prostate cancer cell lines. In the present study we tested the effects of **resveratrol** on the increased proliferation of human AHTO-7 osteoblastic cell line induced by conditioned media (CM) from a panel of carcinoma. . . response of AHTO-7 cells to conditioned media from carcinoma cell lines was diminished (30-71.4% inhibition) upon pretreatment with 0.5 muM **resveratrol**. Highest inhibition was demonstrated for pancreas (BxPC3, Panc-1), breast (ZR75-1) and renal (ACHN) carcinoma cell line supernatants whereas the effect. . . carcinoma (SW620, Colo320DM) cell CM and prostate cancer (PC3, DU 145 and LNCaP) CM was less pronounced. Direct addition of **resveratrol** affected only supernatants of cell lines (<25% inhibition) exhibiting growth stimulatory activity for normal WI-38 **lung fibroblasts**. **Resveratrol** inhibited proliferation of DU145 and LNCaP cells in concentrations exceeding 5 muM, altered cell cycle distribution of all prostate cancer. . . concentrations as low as 0.5 muM, but did not inhibit the production of osteoblastic factors by these lines. In conclusion, **resveratrol** failed to induce ALP activity as marker of osteoblast differentiation in human osteoblastic AHTO-7 cells, however, inhibited their response to. . .

IT Major Concepts
Pharmacology; Tumor Biology

IT Chemicals & Biochemicals
resveratrol: antineoplastic - drug

RN 501-36-0 (**RESVERATROL**)

L3 ANSWER 14 OF 14 FROSTI COPYRIGHT 2003 LFRA on STN
AN 616372 FROSTI
AB A composition comprising **resveratrol** and its analogue is useful

in the treatment of inflammatory respiratory disorders such as bronchitis, asthma, cystic **fibrosis**, bronchiectasis and interstitial **lung** diseases. It can be given by oral or pulmonary administration and is claimed to be more effective than oral, parenteral or pulmonary administration of corticosteroids. **Resveratrol** has known activity in as a cancer chemopreventive agent.

TITLE: Pharmaceutical composition comprising **resveratrol** for treating inflammatory respiratory disorders.
INVENTOR: Donnelly L.E.; Barnes P.J.
PATENT ASSIGNEE: Imperial College Innovations Ltd
SOURCE: European Patent Application
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SUMMARY LANGUAGE: English

TI Pharmaceutical composition comprising **resveratrol** for treating inflammatory respiratory disorders.

AB A composition comprising **resveratrol** and its analogue is useful in the treatment of inflammatory respiratory disorders such as bronchitis, asthma, cystic **fibrosis**, bronchiectasis and interstitial **lung** diseases. It can be given by oral or pulmonary administration and is claimed to be more effective than oral, parenteral or pulmonary administration of corticosteroids. **Resveratrol** has known activity in as a cancer chemopreventive agent.

CT EUROPEAN PATENT; FUNCTIONAL FOODS; HEALTH; INFLAMMATORY RESPIRATORY DISORDERS; PATENT; RESPIRATORY DISORDERS; **RESVERATROL**

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